Clinical pharmacotherapeutics of doxazosin.

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Doxazosin is the latest in a series of highly selective postsynaptic alpha 1-adrenoceptor inhibitors. It is readily absorbed, with high bioavailability and a relatively long plasma half-life, neither of which property is influenced by age. This accounts for the prolonged pharmacologic activity of doxazosin following a single oral dose. Its prime pharmacodynamic activity resides in its ability to counter sympathetic vasoconstriction of the systemic arteriolar resistance vessels and venous capacitance system, which enables the drug to target the major pathophysiologic abnormality in hypertension, i.e., the generalized systemic arteriolar constriction. The widespread vasodilation induced by doxazosin relieves both cardiac preload and afterload and, consequently, reduces left ventricular wall stress and myocardial oxygen consumption. In hypertension, doxazosin reduces blood pressure both at rest and during exercise by reduction of systemic vascular resistance without precipitating substantial reflex cardiac stimulation. The effects are maximal on the standing blood pressure between two and four hours after ingestion; due to doxazosin's relatively slow absorption, postural hypotension is infrequent. Its antihypertensive activity is maintained over 24 hours following a single oral dose, and the optimal dose range is 2 to 8 mg once daily. The antihypertensive efficacy of doxazosin has been shown to be comparable with that of other alpha-adrenoceptor inhibitors, beta-blocking drugs, diuretics, calcium antagonists, and angiotensin-converting enzyme inhibitors. In contrast to other conventional antihypertensive drugs, a unique feature of alpha-adrenoceptor-inhibiting drugs, including doxazosin, is their ability to reduce the plasma concentrations of triglycerides, total cholesterol, and low-density lipoprotein cholesterol and to increase high-density lipoprotein cholesterol concentration. This contrasts with the opposite effect on lipid levels induced by hydrochlorothiazide and atenolol seen in comparative studies. Side effects show no predilection for any organ system, and the overall incidence of such effects compares well with those of other commonly used antihypertensive drugs. This unique combination of antihypertensive efficacy and favorable effect on blood lipid levels indicates that once-daily treatment with doxazosin holds considerable promise in the treatment of hypertension, both from the point of view of its antihypertensive efficacy and also from its primary preventative potential.